IN THE CLAIMS

Please cancel claim 52.

Please amend the claims by substituting the following claims for the corresponding previously pending claims of the same numbers.

11. The method of claim 1, wherein the level of YKL-40 is measured by immunohistochemical staining of cells comprised within said biological sample.

49. The method of claim 47, wherein said biological sample is a sample selected from the group consisting of whole blood, plasma, serum, synovial fluid, cerebrospinal fluid, bronchial lavage, ascites fluid, bone marrow aspirate, pleural effusion, urine, and tumor tissue.

REMARKS

Claims 1-18, 38, 39, 47, 49-52 and 54-62 are currently pending in the application. In the Final Office Action, claims 11, 38 and 49 were rejected under 35 U.S.C. §112 second paragraph as allegedly improper. Claims 11 and 38 were rejected as allegedly unclear in terminology and claim 49 was rejected because it allegedly contains an improper Markush Group. Claim 52 was objected to for insufficient antecedent basis for its limitations. Additionally, Claim 52 was rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Johansen et al. (European Journal of Cancer (1995) 31A(9):1437-1442). Claims 1 and 4-18 were rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by Robbins et al. (U.S. Pat. No. 5,726,061) and claims 1-18, 38-39, 47, 49-52 and 54-62 were rejected under 35 U.S.C. 103(a) as allegedly unpatentable over Johansen in view of Maggio (U.S. Pat. No. 4,828,981) or in view of Harlow (Antibodies: A Laboratory Manual) or in view of Price (WO 95/01995).

Claim 52 is cancelled and claims 11 and 49 are amended herein. No new material has been added through any of these changes and Applicants respectfully request entry of the amendments. In regard to the remaining rejections, Applicants traverse each of them for the reasons explained below.

Information Disclosure State

Please note that a supplemental IDS for this application was filed October 2, 2002. Applicants respectfully request that such IDS be considered for purposes of the Request for Continued Examination filed herewith.

Rejections under 35 U.S.C. § 112 second paragraph

Claim 11

Claim 11 is rejected in the current Office Action as unclear in "that it cannot be determined how cells comprise a biological sample." More specifically, the Office Action disapproves of Applicant's use of the word "comprising" to describe cells as being within a biological sample. Applicants believe the current wording in Claim 11 is correct and proper and respectfully disagree with the Examiner's view of the usage of the word "comprising."

However, for the sake of furthering prosecution, Claim 11 is amended herein to follow the Examiner's suggested wording. Applicants have amended Claim 11 herein solely to expedite prosecution and expressly reserve the right to pursue such un-amended claim in subsequent prosecution and/or subsequent applications.

Because the wording of Claim 11, as amended per the Examiner's suggestion, is proper, Applicants respectfully request that the rejection to Claim 11 be withdrawn.

Claim 49

The current Office Action rejected claim 49 under 35 U.S.C. § 112 second paragraph for containing an improper Markush Group. Claim 49 is amended herein to follow the language helpfully suggested by the Examiner. The amended language is thus properly worded and Applicants respectfully request that the rejection to Claim 49 be withdrawn.

Claim 38

Claim 38 was rejected in the Final office Action under 35 U.S.C. § 112 as allegedly unclear due to recitation of a "possible recurrence" of cancer. In particular, the Action argues that "it is not clear what would be considered a 'possible recurrence' and what would not" and that "it is not clear what standards or measures could be used to determine a 'possible

recurrence'." The Action also questions "how likely must an occurrence be to be 'possible'." Applicants respectfully traverse.

Applicants respectfully point out that the use of the term "possible" in Claim 38 is not indefinite and is, indeed, quite well understood by those of ordinary skill in the art. As is clear from the specification and claims, the word should be given its plain meaning. *See*, e.g., page 15, lines 26-32 and page 16, lines 1-8, which discusses comparison of YKL-40 levels in various biological samples to determine possible recurrence of a cancer. Thus, the term "possible" means "being what . . . may occur according to nature, custom, or manners." *See*, e.g., Merriam-Webster's OnLine (www.m-w.com/home.htm) at "possible."

Applicants also point out that the "standards or measures . . . used to determine a 'possible recurrence'" are given in the specification. *See*, e.g., page 15, lines 26-32 and page 16, lines 1-8. For example, a patient who does not have an elevation of YKL-40 at the time of surgery but does show an increased YKL-40 level at any time after surgery, shows an indication of a possible recurrence of the cancer. The specification also makes clear that YKL-40 levels used as indicia of possible recurrence of cancer can be measured, e.g., relative to levels in normal health people, relative to baseline YKL-40 levels for a patient (e.g., prior to surgery, during surgery, immediately after surgery), etc. Thus, the metes and bounds of "possible recurrence" are clearly indicated in the specification as filed. It should be noted that the present claim is NOT drawn to a "probability" of recurrence of cancer, but rather is drawn to a "possibility" of recurrence. The question of "how likely must an occurrence be" is not really pertinent to the claim. Because the wording of Claim 38 is not indefinite under 35 U.S.C. §112, Applicants respectfully request withdrawal of the rejection.

Claim 52

The Final Office Action also rejects Claim 52 based upon alleged insufficient antecedent basis for the limitation of "breast cancer" in the claim. Claim 52 is cancelled with entry of this amendment thereby obviating this rejection.

Rejections under 35 U.S.C. § 102(b)

Claim 52

Claim 52 was also rejected in the current Office Action as being anticipated by Johansen et al., European Journal of Cancer, 1995, Vol. 31A, No. 9, pp. 1437-1442. As stated above, Claim 52 is cancelled herein, thus, obviating this rejection.

Rejections under 35 U.S.C. § 102(e)

Claims 1 and 4-18

Claims 1 and 4-18 were rejected in the Final Office Action as allegedly being anticipated by Robbins et al., U.S. Pat. No. 5,726,061 filed October 8, 1996 and issued March 10, 1998. Applicants respectfully traverse.

The Office Action alleges that Robbins teaches a method for screening for colorectal cancer by measuring levels of HCgp-39 (also called YKL-40), wherein the subtypes of colorectal are "inherently" included. The Office Action also alleges that Robbins teaches the method for monitoring the cancer, wherein a method for estimating the survival is "inherently" taught. As support for such allegations, the Office Action directs attention to the abstract and col. 3, second paragraph of Robbins.

For anticipation under 35 U.S.C. §102(e), "[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *See*, M.P.E.P. §2131 quoting *Verdegaal Bros. v. Union Oil Co. of California*, 2 USPQ 2d 1051, 1053. The basic standard for anticipation by inherency is set forth in *Continental Can Co. v. Monsanto Co.*, *see*, M.P.E.P. §2131.01:

> Anticipation by inherency requires that 1) the missing descriptive subject matter be "necessarily present" in the prior art reference and that 2) it would be so recognized by persons of ordinary skill in the art. *Continental Can Co. v. Monsanto Co.*, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991).

Applicants point out that neither of the above requirements are met by Robbins with respect to the current claims. The fact that Robbins allegedly contains methods for early detection of colorectal cancer and for monitoring of disease status of colorectal cancer does not

equate with an inherent step or act of estimating the survival expectancy of a cancer patient as is done in the claimed invention. One of skill in the art would understand that monitoring a colorectal cancer (Robbins) does not necessarily entail estimating survival expectancy (the claimed invention). As is apparent from column 3, lines 23-24, Robbins focuses on YKL-40 levels of indications of treatment efficacy. Determination or estimation of survival expectancy is a separate issue from measurement of treatment efficacy. For example, treatment efficacy can quite easily be determined without any determination/estimation of survival expectancy (e.g., measuring whether a treatment is effective or ineffective does not necessarily give one an estimation on the expectancy of survival of a patient). Furthermore, Robbins' oblique language at column 2 lines 30-36 mentioning predicting therapeutic outcome or disease prognosis are, again, quite different from the present claims which are drawn to estimation of survival expectancy. One can easily envision situations comprising tracking efficacy of a treatment (therapeutic outcome) without estimating survival expectancy of the patient receiving such treatment. Such questions are based on different viewpoints (i.e., treatment based viewpoint as opposed to patient based viewpoint). Also, one can envision numerous situations wherein disease prognosis (tracking progressive spread of disease, etc.) does not entail an estimate of survival expectancy. Again, such methods are approached from different viewpoints – from a disease tracking point of view versus a patient survival expectancy point of view.

"The fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic." *See*, M.P.E.P. §2112, citing *In re Rijckaert*, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993), emphasis in original. This quote leads back to the standard iterated in *Continental Can* (*see*, above) in that in order for something to be inherent in the prior art it must be "necessarily present." It would be clear to one skilled in the art that Robbins can be practiced without estimating a survival expectancy of a cancer patient, hence, such is not inherent in Robbins. Thus, Robbins does not teach each element of the present claims and therefore is not a proper basis for a rejection under 35 U.S.C. 102. Applicants respectfully request that such rejection be withdrawn.

Rejections under 35 U.S.C. § 103(a)

Claims 1-18, 47, 49-52 and 54-62

The current Office Action rejected Claims 1-18, 47, 49-52 and 56-62 under 35 U.S.C. §103(a) as allegedly unpatentable over Johansen et al. (European Journal of Cancer, 1995, vol. 31a, No. 9, pp. 1437-1442) in view of Maggio et al (U.S. Pat. No. 4,828,981, issued May 9, 1989) or in view of Harlow et al. (Antibodies, A Laboratory Manual, Cold Spring Harbor Laboratory, 1988, pages 148-212) or in view of Price et al. (WO 95/01995, January 19, 1995). Applicants respectfully traverse.

Three requirements must be met for a prima facie case of obviousness from combined references. First, there must be a motivation to modify the reference or combine the teachings to produce the claimed invention. M.P.E.P. §2143.01. Second, there must be a reasonable expectation of success. M.P.E.P. §2143.02. Third, the prior art reference(s) must teach all of the limitations of the claims. M.P.E.P. §2143.03. Furthermore, the teaching or suggestion to combine and the expectation of success must both be found in the prior art and not based upon the disclosure of the Applicants. M.P.E.P. §2142.

Applicants respectfully point out that none of these requirements have been met for a prima facie showing of obviousness.

First, and quite importantly, all limitations of the current claims are not present within the combined references. Therefore, not all of the limitations of the current claims have been shown to be in the combination of art at issue and, thus, an obviousness rejection is not proper. For example, current Claims 1 and 47 disclose numerous cancer types (e.g., lung, bronchus, etc.) which a cancer patient whose survival expectancy is to be estimated may have. The recited cancers are found nowhere in the cited references. As pointed out in Applicant's previous response, Johansen et al. concerns itself with breast cancer. Likewise, Price et al. solely concerns itself with breast cancer. Additionally, as helpfully pointed out by the Examiner, neither Maggio nor Harlow are concerned with cancer types at all, but instead are concerned with antibodies and competitive immunoassays.

Thus, the Office Action has failed to establish a prima facie case of obviousness, since nowhere in any of the cited references are the recited cancer types shown. The Final Office Action alleges that because YKL-40 is over-expressed in pathologies with tissue remodeling and

appears to be a glycosidase contributing to metastasis that such language somehow equals, or adds up to, all of the limitations found in Claims 1 and 47. This is not the case. The limitations of Claims 1 and 47 (and hence their dependencies as well) are not present, either inherently or expressly, within the cited references. Again, the Office Action has failed to create a prima facie case of obviousness because not all of the limitations of the current claims are found within the cited references.

Secondly, the cited references do not contain a motivation to modify or combine the teachings to produce the current invention. The Final Office Action states that Johansen indicates at pages 1441-1442 that "it is likely that YKL-40 will be useful for monitoring other cancers." However, it is well established that such a statement is insufficient to establish specific motivation to combine the references at issue. The references must contain specific reasons for combination – not an invitation to experiment to see whether a hoped for result may occur. Put another way, the Examiner's proposed rationale for combination is an attempt to establish that the claimed invention would have been obvious to try, rather than obvious, a standard repeatedly struck down by the courts as ever providing a legitimate basis for establishing obviousness. *See*, e.g., *Ex Parte Erlich*, 3 USPQ2d 1011 (BPAI 1986); *In re Geiger*, 2 USPQ2d 1276 (Fed. Cir. 1987); *In Re Dow*, 5 USPQ2d 1529 (Fed. Cir. 1988); and *In Re Eli Lilly & Co.* 14 USPQ2d 1741, 1743 (Fed. Cir. 1990). As the court has repeatedly held, one may not establish motivation by pointing to a passage that invites experimentation to see if something will work, which is precisely as the Examiner has done in the present case.

Thirdly, there is no reasonable expectation of success, fully achieving the desired invention, in the combined references. The Final Office Action alleges that Johansen provides a reasonable expectation of success because of the wording on pages 1441-1442. However, once again, the combined references do not even teach every element of the current claims, let alone provide any reasonable demonstration that the claimed invention would work, had it been proposed.

Because of the foregoing reasons, a rejection of obviousness for claims 1 and 47 (and hence their dependent claims 2-18, 49-52, and 56-62) is improper and Applicants respectfully request its withdrawal.

CONCLUSION

The current Amendments present no new matter. Applicants believe that the amendments to the claims and the arguments herein overcome all outstanding rejections. The rejections, accordingly, must be withdrawn.

In view of the foregoing, Applicants believe all claims now pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

In the event that any issues of substance are perceived to remain, Applicants request that the Examiner contact the undersigned at 510-337-7871 to arrange for a telephonic interview, prior to preparation of any additional Office Action.

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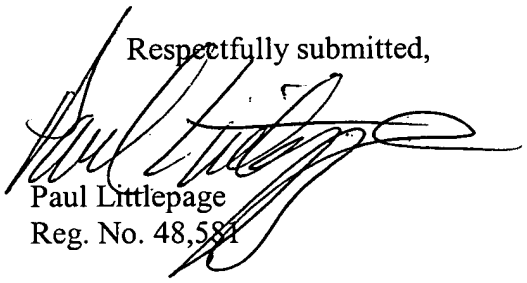
Respectfully submitted,



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APPENDIX A

"MARKED UP" CLAIMS ILLUSTRATING THE AMENDMENTS MADE TO THE CLAIMS OF 09/164,862 WITH ENTRY OF THIS AMENDMENT

11. (Amended) The method of claim 1, wherein the level of YKL-40 is measured by immunohistochemical staining of cells **comprised within**[comprising] said biological sample.

49. (Amended) The method of claim 47, wherein said biological sample is a sample **selected from the group consisting of** whole blood, plasma, serum, synovial fluid, cerebrospinal fluid, bronchial lavage, ascites fluid, bone marrow aspirate, pleural effusion, urine, **and**[or] tumor tissue.

52. Cancelled.

APPENDIX B

CLAIMS PENDING IN 09/164,862 WITH ENTRY OF THIS AMENDMENT

1. A method for estimating survival expectancy of a cancer patient, said method comprising:

(a) obtaining a biological sample comprising YKL-40 from a cancer patient having at least a preliminary diagnosis of a cancer selected from the group consisting of a lung cancer, a bronchus cancer, a colorectal cancer, a prostate cancer, a pancreas cancer, a stomach cancer, an ovarian cancer, a urinary bladder cancer, a brain or central nervous system cancer, a peripheral nervous system cancer, an esophageal cancer, a cervical cancer, a melanoma, a uterine or endometrial cancer, a cancer of the oral cavity or pharynx, a liver cancer, a kidney cancer, a biliary tract cancer, a small bowel or appendix cancer, a salivary gland cancer, a thyroid gland cancer, an adrenal gland cancer, an osteosarcoma, a chondrosarcoma, a liposarcoma, a testes cancer, and a malignant fibrous histiocytoma;

(b) measuring the level of YKL-40 in said sample and comparing the sample YKL-40 level to the YKL-40 level found in the same sample from a normal healthy human wherein a sample YKL-40 level in excess of YKL-40 levels in the same sample from a normal healthy human indicates a reduced survival expectancy compared to patients with normal YKL-40 level.

2. The method of claim 1, wherein said patient has a diagnosis of prostate cancer.

3. The method of claim 1, wherein said patient has a diagnosis of lung cancer.

4. The method of claim 1, wherein said patient has a diagnosis of a colorectal cancer.

5. The method of claim 4, wherein said patient is diagnosed with a Duke's stage A colorectal cancer.

6. The method of claim 4, wherein said patient is diagnosed with a Duke's stage B colorectal cancer.

7. The method of claim 4, wherein said patient is diagnosed with a Duke's stage C colorectal cancer.

8. The method of claim 4, wherein said patient is diagnosed with a Duke's stage D colorectal cancer.

9. The method of claim 1, wherein said biological sample is a primary tumor or a tissue affected by the cancer.

10. The method of claim 1, wherein said biological sample is a sample selected from the group consisting of whole blood, plasma, serum, synovial fluid, cerebrospinal fluid, bronchial lavage, ascites fluid, bone marrow aspirate, pleural effusion, urine, and tumor tissue.

11. The method of claim 1, wherein the level of YKL-40 is measured by immunohistochemical staining of cells comprised within said biological sample.

12. The method of claim 11, wherein said cells are tumor tissue cells.

13. The method of claim 1, wherein the level of YKL-40 is measured using an immunoassay.

14. The method of claim 13, wherein said immunoassay is a competitive immunoassay.

15. The method of claim 13, wherein said immunoassay is an ELISA.

16. The method of claim 13, wherein said immunoassay is a radioimmunoassay (RIA).

17. The method of claim 13, wherein said immunoassay uses a polyclonal anti-YKL-40 antibody.

18. The method of claim 13, wherein said immunoassay uses a monoclonal anti-YKL-40 antibody.

38. A method to screen for recurrence of a cancer after removal of a primary tumor, said method comprising:

(a) obtaining a biological sample comprising YKL-40 from a cancer patient following removal of a primary tumor selected from the group consisting of a lung cancer, a bronchus cancer, a colorectal cancer, a prostate cancer, a pancreas cancer, a stomach cancer, an ovarian cancer, a urinary bladder cancer, a brain or central nervous system cancer, a peripheral nervous system cancer, an esophageal cancer, a cervical cancer, a melanoma, a uterine or endometrial cancer, a cancer of the oral cavity or pharynx, a liver cancer, a kidney cancer, a biliary tract cancer, a small bowel or appendix cancer, a salivary gland cancer, a thyroid gland cancer, an adrenal gland cancer, an osteosarcoma, a chondrosarcoma, a liposarcoma, a testes cancer, and a malignant fibrous histiocytoma; and

(b) measuring a level of YKL-40 in said sample and comparing the sample YKL-40 level to the YKL-40 level found in the same sample in a normal healthy human wherein a sample YKL-40 level in excess of YKL-40 levels in a normal healthy human indicates a possible recurrence of said cancer.

39. The method of claim 38, wherein said method is repeated at a multiplicity of instances after removal of said primary tumor.

47. A method of screening for a cancer, in a mammal, said method comprising:

(a) obtaining a biological sample comprising YKL-40 from said mammal;

(b) measuring the level of YKL-40 in said sample and comparing the level to the YKL-40 level found in the same sample from a normal healthy mammal, wherein a

statistically significant difference in YKL-40 level in the sample being tested compared to the sample from a normal healthy mammal indicates the presence of a cancer selected from the group consisting of a lung cancer, a bronchus cancer, a prostate cancer, a pancreas cancer, a stomach cancer, an ovarian cancer, a urinary bladder cancer, a brain or central nervous system cancer, a peripheral nervous system cancer, an esophageal cancer, a cervical cancer, a melanoma, a uterine or endometrial cancer, a cancer of the oral cavity or pharynx, a liver cancer, a kidney cancer, a biliary tract cancer, a small bowel or appendix cancer, a salivary gland cancer, a thyroid gland cancer, an adrenal gland cancer, an osteosarcoma, a chondrosarcoma, a liposarcoma, a testes cancer, and a malignant fibrous histiocytoma.

49. The method of claim 47, wherein said biological sample is a sample selected from the group consisting of whole blood, plasma, serum, synovial fluid, cerebrospinal fluid, bronchial lavage, ascites fluid, bone marrow aspirate, pleural effusion, urine, and tumor tissue.

50. The method of claim 47, wherein said cancer is selected from the group consisting of a breast cancer, a lung cancer, and a prostate cancer.

51. The method of claim 47, wherein said cancer is selected from the group consisting of a stomach cancer, a cervical cancer, an ovarian cancer, and a malignant melanoma.

54. The method of claim 50, wherein said cancer is a prostate cancer.

55. The method of claim 50, wherein said cancer is a lung cancer.

56. The method of claim 47, wherein said mammal is a human.

57. The method of claim 47, wherein the level of YKL-40 is measured using an immunoassay.

58. The method of claim 57, wherein said immunoassay is a competitive immunoassay.

59. The method of claim 57, wherein said immunoassay is an ELISA.

60. The method of claim 57, wherein said immunoassay is a radioimmunoassay (RIA).

61. The method of claim 57, wherein said immunoassay uses a polyclonal anti-YKL-40 antibody.

62. The method of claim 57, wherein said immunoassay uses a monoclonal anti-YKL-40 antibody.